

What is claimed is:

1. A self-replicating episomal DNA expression vector for expressing a gene of interest in a host cell in a tissue-restricted manner, the vector comprising:
- (a) a self-replicating origin of replication; and
 - (b) an LCR, or component thereof, which when operatively linked to a gene of interest and present in a host cell directs expression of said gene in a tissue-restricted manner.
2. The self-replicating episomal DNA expression vector of claim 1, further comprising a gene of interest operatively linked to the LCR, or component thereof.
3. The self-replicating episomal DNA expression vector of claim 2 wherein the component of an LCR is a component of the β -globin LCR consisting essentially of HS3.
4. The self-replicating episomal DNA expression vector of claim 2 wherein the LCR, or component thereof is the β -globin LCR or component thereof excluding site HS2.
5. The self-replicating episomal DNA expression vector of claim 2 wherein the component of an LCR is a component of the β -globin LCR consisting essentially of HS3 and HS4.
6. The self-replicating episomal DNA vector of claim 1, wherein the origin of replication is a viral origin of replication.

7. The self-replicating episomal DNA expression vector of claim 6 wherein the viral origin of replication is an origin of replication from Epstein-Barr virus.

8. The self-replicating episomal DNA expression vector of claim 1, further comprising a sequence encoding a replication factor required for replication of the expression vector in a host cell.

9. The self-replicating episomal DNA expression vector of claim 8 wherein the sequence encoding the replication factor is selected from the group consisting of a sequence encoding EBNA-1 of Epstein-Barr virus, a sequence encoding E1 of papilloma virus, and a sequence encoding E2 of papilloma virus.

10. The self-replicating episomal DNA expression vector of claim 1, further comprising an antibiotic resistance gene for selecting cells in culture stably transfected with the expression vector.

11. The self-replicating episomal DNA expression vector of claim 1, further comprising a eukaryotic transcription termination sequence placed between the LCR and the gene of interest and operative to prevent transcription therebetween.

Sub D1
A 12. A pair of vectors comprising a self-replicating/episomal DNA expression system for expressing a gene of interest in a host cell in a tissue-restricted manner, the pair of vectors comprising:

- i. a first vector comprising
- (a) an origin of replication;
 - (b) an LCR, or component thereof, which when operatively linked to a gene of interest and present in a host cell directs expression of said gene in a tissue-restricted manner; and
 - (c) a cloning site for a gene of interest; and
- ii. a second vector comprising
- (a) ^{said} an origin of replication; and
 - (b) a sequence encoding a replication protein, said replication protein being necessary for replication of said origin of replication.

13. The pair of vectors of claim 12, further comprising a gene of interest operatively linked to the LCR, or component thereof.

Sub D3
A 14. The pair of vectors of claim 12 wherein the component of an LCR is a component of the β -globin LCR consisting essentially of HS3.

15. The pair of vectors of claim 12 or claim 13 wherein the LCR, or component thereof is the β -globin LCR or component thereof excluding site HS2.

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16. The pair of vectors of claim 12 wherein the component of an LCR is a component of the β -globin LCR ~~consisting essentially of HS3 and HS4.~~

17. The pair of vectors of claim 12 wherein the origin of replication is a viral origin of replication .

18. The pair of vectors of claim 17, said viral origin of replication being from Epstein-Barr virus

19. The pair of vectors of claim 12 wherein the sequence encoding the replication factor is selected from the group consisting of a sequence encoding EBNA-1 of Epstein-Barr virus, a sequence encoding E1 of papilloma virus, and a sequence encoding E2 of papilloma virus.

20. The pair of vectors of claim 12, wherein each said first and second vector further comprising, individually, an antibiotic resistance gene for selecting cells in culture stably transfected with the expression vector.

21. The pair of vectors of claim 12 wherein said first vector further comprising a eukaryotic transcription termination sequence placed between the LCR and the cloning site for the gene of interest.

22. A method for expressing a gene of interest in cells of a specific tissue-type comprising administering a self-replicating episomal DNA expression vector of claim 1 or a pair of vectors of claim 12 to a mammal.

23. A method of obtaining persistent, tissue-specific expression of a gene of interest in a host cell in culture, comprising culturing a host cell transfected with the vector of claim 1 or the pair of vectors of claim 12.

24. A transgenic animal containing cells which contain the expression vector of claim 1 or the pair of vectors of claims 12.

25. A method for identifying an LCR or component thereof which when comprised in an episomal DNA expression vector, operatively linked to a gene of interest, and present in a host cell, directs expression of said gene in a tissue-restricted manner, comprising:

- i. testing the LCR or component thereof by transfecting an episomal vector containing the candidate LCR or component thereof operatively linked to a marker gene into a cell line in which the LCR when integrated is active and also into a cell line in which the LCR when integrated is inactive; and
- ii. identifying the LCR or component thereof which is only active in the cell line in which the LCR when integrated is active.

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